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Validation of seven type 2 diabetes mellitus risk scores in a population-based cohort. The Colaus study

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ABSTRACT

Objective: Assess the validity of seven type 2 diabetes mellitus (T2DM) risk scores in predicting the 10-year incidence of T2DM in a Swiss population based study.

Methods: prospective study including 5131 participants (55% women, age range 35 to 75 years) living in Lausanne, Switzerland. The baseline survey was conducted between 2003 and 2006 and average follow-up was 10.9 years. Five clinically-based (Balkau, Kahn clinical, Griffin, Swiss diabetes association and Findric) and two clinically and biologically based scores (Kahn CB and Wilson) were tested.

Results: 405 (7.9%) participants developed T2DM. The overall prevalence of participants at high risk ranged from 13.7% for the Griffin score to 43.3% for the Balkau score. Prevalence of participants at high risk among those who developed T2DM ranged from 34.6% for the Griffin score to 82.0% for the Kahn CB score. The Kahn CB score had the highest area under the ROC [value and 95% confidence interval: 0.866 (0.849-0.883)], followed by the Findrisc [0.818 (0.798-0.838)] while the Griffin score had the lowest [0.740 (0.718-0.762)]. Except for the Griffin and the Kahn C scores (for sensitivity) and the Balkau score (for specificity), sensitivities and specificities were above 70%. The numbers needed to screen ranged between 15.5 for the Kahn CB score to 36.7 for the Griffin score.

Conclusion: The Kahn (CB) and the Findrisc performed best of all scores. Findrisc could be used in the epidemiological setting, while the need of blood sampling for the Kahn (CB) score restricts its use to a more clinical setting.

Keywords: type 2 diabetes mellitus; risk scores; prospective study; epidemiology

INTRODUCTION:

The prevalence of type 2 diabetes mellitus (T2DM) is increasing worldwide (1). In Switzerland, one out of sixteen persons aged between 35 and 75 years has diabetes mellitus, and almost one third of diabetic subjects is unaware of their status (2) T2DM carries a considerable economic burden (3) as patients with T2DM are at higher risk of developing cardiovascular, neurological, renal and ophthalmic complications. Hence, early diagnosis of T2DM is of major importance as the outcome of the disease can be modified through medical care and lifestyle changes (4). The identification of subjects at high risk of developing T2DM might also be cost-effective by reducing the incidence of T2DM (5). Therefore, multiple predictive risk scores have been developed to detect patients at high risk of developing T2DM (6). Such scores rely mainly on anamnestic and clinical information such as personal or family history and on simple measurements such as blood pressure, weight or waist. Some scores use additional blood markers such as fasting glucose, cholesterol and triglycerides. While scores including blood markers tend to perform better, their cost is higher (6). Further, most scores have been validated in selected populations, and their application in other settings or populations is not warranted.

In a previous study, we assessed the 5.5-year predictive capacity of seven T2DM risk scores in a prospective, population-based sample (7). As many scores were originally developed using longer follow-up times, a further validation was deemed necessary. Hence, in this study, we aimed to validate the seven above-mentioned T2DM risk scores over a 10-year follow-up. Our initial hypothesis was that the predictive capacity of each score would not change significantly in a longer follow-up.

METHODS

The Colaus study

The sampling procedure of the CoLaus cohort has been described previously (8) and further details can be obtained in www.colaus-psycolaus.ch. Briefly, the source population was defined as all subjects aged between 35 and 75 years registered in the population register of the city of Lausanne. The register includes all subjects living in this city for more than 90 days. A simple, non-stratified random sample of 19'830 subjects (corresponding to 35% of the source population) was drawn and the selected subjects were invited to

participate by letter. If no answer was obtained, a second letter was sent, and if no answer was obtained, the subjects were contacted by phone. Recruitment began in June 2003 and ended in May 2006, enrolling 6733 total participants who underwent an interview, a physical exam, and a blood analysis. The first follow-up was performed between April 2009 and September 2012, 5.6 years on average (media 5.4 years, range 4.5-8.8) after the collection of baseline data; the second follow-up was performed between May 2014 and April 2017, 10.9 years on average (median 10.7, range 8.8-13.6) after the collection of baseline data. The information collected was similar to that collected in the baseline examination.

Data collection

Participants were asked to attend an outpatient clinic at Centre Hospitalier Universitaire Vaudois in the morning, after an overnight fast. Socio-demographic, history of disease (personal and familiar) and lifestyle data was collected by questionnaire. Smoking was categorized as never, former and current; alcohol consumption was assessed by the number of alcoholic drinks (i.e. glasses of wine, cans of beer or shots of spirit) consumed the last seven days and categorized into none, moderate (1-13 units/week), high (14-27 units/week) and very high (28+ units/week). Educational level was categorized as low (primary), middle (apprenticeship), upper middle (high school), and high (university) for highest completed level of education. Physical activity was defined by exercising at least twice per week for at least 20 minutes per session. Prescribed and over-the-counter medicines were collected by questionnaire.

Body weight and height were measured with participants barefoot and in light indoor clothes. Body weight was measured in kilograms to the nearest 100 g using a Seca® scale (Hamburg, Germany). Height was measured to the nearest 5 mm using a Seca® (Hamburg, Germany) height gauge. Waist circumference was measured mid-way between the lowest rib and the iliac crest using a non-stretchable tape and the average of two measurements was taken. Blood pressure (BP) and resting heart rate were measured thrice using an Omron® HEM-907 automated oscillometric sphygmomanometer after at least a 10-minute rest in a seated position. Different sized cuffs were available to take into account arm cirumference and the average of the last two measurements was used.

Venous blood samples (50 mL) were drawn in the fasting state. Biological assays were performed at the clinical laboratory of the Lausanne university hospital within 2 hours of blood collection. Glucose was

assessed by glucose dehydrogenase with a maximum inter- and intra-assay CV of 2.1% and 1.0%, respectively; HDL-cholesterol by CHOD-PAP + PEG + cyclodextrin (3.6%-0.9%); triglycerides by GPO-PAP (2.9%-1.5%), and uric acid by uricase-PAP (1.0%-0.5%). Glycated hemoglobin was measured by high performance liquid chromatography (HPCL) using Bio-Rad, D-10^{TM} system, with measurement range 3.8% (at 18 mmol/mol) to 18.5% (at 179 mmol/mol).

Diabetes risk scores

Seven DM risk scores were considered: 1) the FINDRISC (9) ; 2) the Swiss Diabetes Association (SDAS) (10) ; 3) the clinical and clinico-biological scores by Kahn et al., respectively (11); 4) the clinico-biological risk score by Wilson et al. (12); 5) the clinical risk score by Balkau et al. (13), and 6) the clinical risk score by Griffin et al. (14). The details of each score are summarized in **supplemental table 1**.

The FINDRISC score was derived from the 10 year follow-up FINRISK study consisting of 4435 participants (9) and consists of seven variables. The Swiss Diabetes Association risk score (SDAS) is adapted from the FINDRISC, using familial history of diabetes as an additional variable. The risk scores by Kahn et al (11) were derived in a cohort of 15'792 adults followed up during 10 years. The clinical risk score (C) consists of nine variables, while the clinic-biological risk score (CB) has four additional biological markers. The clinic-biological risk score of Wilson et al. (12) was derived from the Framingham Offspring Study, where 3140 participants were followed up 8 years; the score consists of six variables (three clinical and three biological). The clinical risk score of Balkau et al (13) was derived from the DESIR cohort, where 3817 participants were followed for nine years; it consists of four variables. Finally, the score of Griffin et al (14) was derived from a cross-sectional study consisting of 1077 participants, and is composed of five clinical variables.

The FINDRISC, SDAS, Kahn (C and B), Wilson and Balkau scores are based on a sum of allocated number of points per variable. For the FINDRISC and SDAS, nutritional variables and familial history of diabetes for second-degree parents were not available at baseline; thus, the threshold was reduced by 1 point. The Griffin score uses a regression equation to calculate the probability of developing T2DM. As no threshold had been proposed in the original study, a 37% probability was used to identify high-risk individuals, as proposed elsewhere (11).

Outcome

The primary outcome was T2DM, defined as fasting blood glucose ≥7.0 mmol/l or taking insulin or oral antidiabetic medication.

Exclusion criteria

The original inclusion criteria were: 1) written informed consent; 2) willingness to take part in the examination and to provide blood samples; 3) French language ability. For this study, we added the following exclusion criteria: 1) diabetes (type 1 or 2) at baseline; 2) no follow-up (first or second); 3) missing variables to compute the scores and 4) no outcome data.

Ethical statement

The institutional Ethics Committee of the University of Lausanne, which afterwards became the Ethics Commission of Canton Vaud (www.cer-vd.ch) approved the baseline CoLaus study (reference 16/03, decisions of 13th January and 10th February 2003); the approval was renewed for the first (reference 33/09, decision of 23rd February 2009) and the second (reference 26/14, decision of 11th March 2014) follow-up. The study was performed in agreement with the Helsinki declaration and its former amendments, and in accordance with the applicable Swiss legislation. All participants gave their signed informed consent before entering the study.

Statistical analysis

Statistical analyses were conducted using Stata version 15.1 for Windows (Stata Corp, College Station, Texas, USA). Participants characteristics were expressed as number (percentage) for categorical variables or as average±standard deviation for continuous variables. Between-group comparisons were performed using chi-square or Fisher's exact test for categorical variables and student's t-test or Kruskal-Wallis test for continuous variables.

Risk scores were expressed as median and [interquartile range]. The diagnostic capacity of the different risk scores was assessed by the AUC [area under the ROC (receiver operating characteristic) curve] and corresponding 95% confidence intervals (CI). Comparisons of the AUC between scores were performed using the **roccomp** command of Stata. Sensitivity, specificity, positive and negative predictive values and their corresponding 95% CIs were computed using incident T2DM as gold standard. The number needed to screen (NNS) to detect one case of T2DM was computed as the total number of participants screened divided by the

number of detected T2DM cases (i.e. true positives). Statistical significance was assessed for a two-sided test with $p<0.05$.

RESULTS

Characteristics of participants

Of the initial 6733 participants 5131 (76.2%) were retained for analysis. The reasons for exclusion are summarized in **figure 1** and the characteristics of the included and the excluded participants are summarized in the **supplementary table 2**. Included participants were younger; had lower waist and BMI; had lower prevalence of hypertension and family history of diabetes; had lower levels of fasting plasma glucose and uric acid than excluded ones. Included participants also had higher caffeine and alcohol consumption and higher levels of physical activity and HDL than excluded ones.

Incidence of T2DM

At the second follow-up, 405 (7.9%) participants developed T2DM. The baseline characteristics of the participants who developed and did not develop T2DM are summarized in **table 2**. Participants who developed T2DM were more frequently male, were older, had higher waist and BMI, a higher prevalence of family history of diabetes and hypertension or of being former or current smokers, had a higher alcohol consumption and higher levels of fasting plasma glucose, triglycerides, HDL and uric acid.

Performance of risk scores

The median score and the prevalence of participants at high risk of developing T2DM overall and according to (non)development of T2DM are provided in **table 2** for each risk score. The overall prevalence of participants at high risk ranged from 13.7% for the Griffin score to 43.3% for the Balkau score. Prevalence of participants at high risk among those who developed T2DM ranged from 34.6% for the Griffin score to 82.0% for the Kahn CB score (**table 2**).

The AUC, sensitivity, specificity, positive and negative predictive values and the number needed to screen to detect one case of T2DM are summarized in **table 3** for each risk score. The AUCs for each score are also provided in **Figure 2** and the results of the bivariate comparisons of the AUCs are provided in **table 4**. The Kahn CB score had the highest AUC while the Griffin score had the lowest. Except for the Griffin and the Kahn C scores (for sensitivity) and the Balkau score (for specificity), sensitivities and specificities were above 70%.

Positive predictive values were below 25%, while negative predictive values were above 90%. The numbers needed to screen ranged between 15.5 for the Kahn CB score to 36.7 for the Griffin score (**table 3**).

DISCUSSION

Out of the seven diabetes risk scores evaluated, the two with the highest AUC were the Kahn et al (CB), which includes biological variables, and the Findrisc, which is based on clinical data only. This finding is comparable to what was reported previously using a shorter follow-up period (5.5 vs. 10.9 years) (7). Importantly, our results confirm our hypothesis that the predictive value of a diabetes risk score does not change significantly when follow-up times shorter than the ones used for the original validation are used.

Diabetes risk scores

The Kahn (CB) score showed the best metrics, a finding already reported previously (7). Several reasons might explain this performance: first, it was developed using a large sample size (12'729) and included four blood markers. Although the inclusion of blood markers might improve the predictive capacity of the score, it also makes it more expensive to use either for mass screening or for everyday clinical use. Hence, it applicability in settings with limited health resources will be reduced. The Wilson score also includes biological markers but, contrary to the Kahn CB, its predictive capacity was rather low and its AUC was comparable to the clinical version of the Kahn score.

The Findrisc score ranked second highest among all scores. Contrary to the Kahn (CB) score, the Findrisc score is based solely on clinical data and can thus be applied in screening campaigns or in communities with limited health resources. Importantly, although the complete version of the Findrisc score could not be used in this study, still the reduced version performed well, suggesting that the performance of the complete version, if computable, could even be better. Further, the SDAS, which is based on the Findrisc, also showed an adequate performance, albeit with a lower AUC than the Findrisc. The likely reason is an arbitrary addition of 5 points for family history of diabetes on the SDAS, which does not seem to improve its performance. The Balkau score had the lowest number of components. Although this small number of items might facilitate its applicability in public health or in clinical practice, its predictive capacity was modest, and it led to a very high number of participants classified as being "at risk". Finally, the Griffin score had the lowest prediction capacity. A probable explanation is that it was developed in a cross-sectional setting, whereas the other scores were

developed in a prospective setting. Overall, our results indicate that a prospective setting is paramount to adequately derive and validate a risk prediction score. Indeed, most scores perform well in the populations they were developed in, but their predictive value drops when applied to a different cohort. Hence, externally validating predictive scores on different populations is essential to assess their generalizability and performance.

Strengths and limitations

The main strength of our study is that we used a follow-up time similar to the one the scores were developed for. The second strength is the relatively large sample size, which provided an adequate number of incident events.

We also acknowledge several limitations. Firstly, no nutritional data was collected at baseline; hence, we had to adapt the threshold of the Findrisc and SDAS scores by reducing the threshold by one unit, a procedure also performed in our previous study (7). Still, despite this limitation, both the Findrisc and the SDAS scores performed better than other scores. Secondly, the CoLaus study includes a majority of Caucasian subjects lving in a high-income country and in an urban setting; hence, generalizability to other ethnicities or other settings might not be warranted. It would be important that our study be replicated in other cohorts to validate the robustness of our findings. Thirdly, we lost approximately 15% of our baseline cohort during the first and the second follow-up, which might have reduced the number of incident T2DM events. Still, this impacted equally all scores and would not change the conclusions of the study.

Conclusion

The Kahn (CB) and the Findrisc performed best of all scores. Findrisc could be used in the epidemiological setting, while the need of blood sampling for the Kahn (CB) score restricts its use to a more clinical setting.

FUNDING

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AUTHORS CONTRIBUTIONS

GW revised the article for important intellectual content. PMV had full access to the data and is the guarantor of the study.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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Figure legends

Figure 1: exclusion criteria. Results are expressed as number of participants and (percentage) using the baseline number of subjects as denominator.

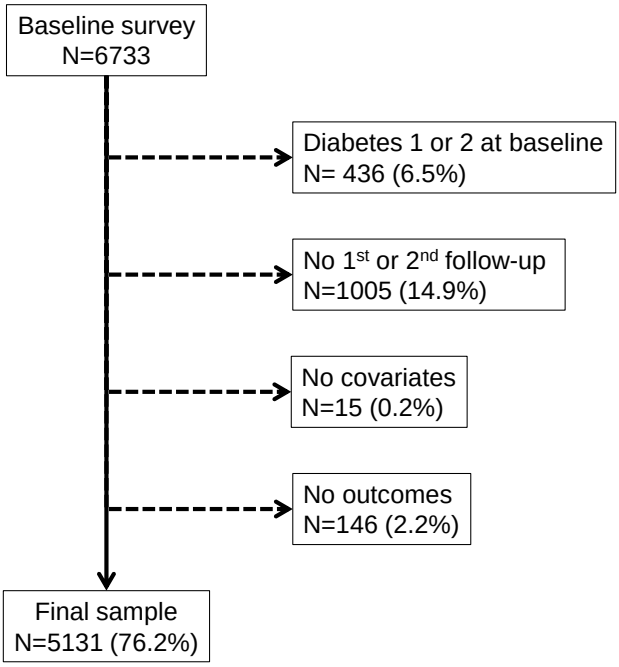
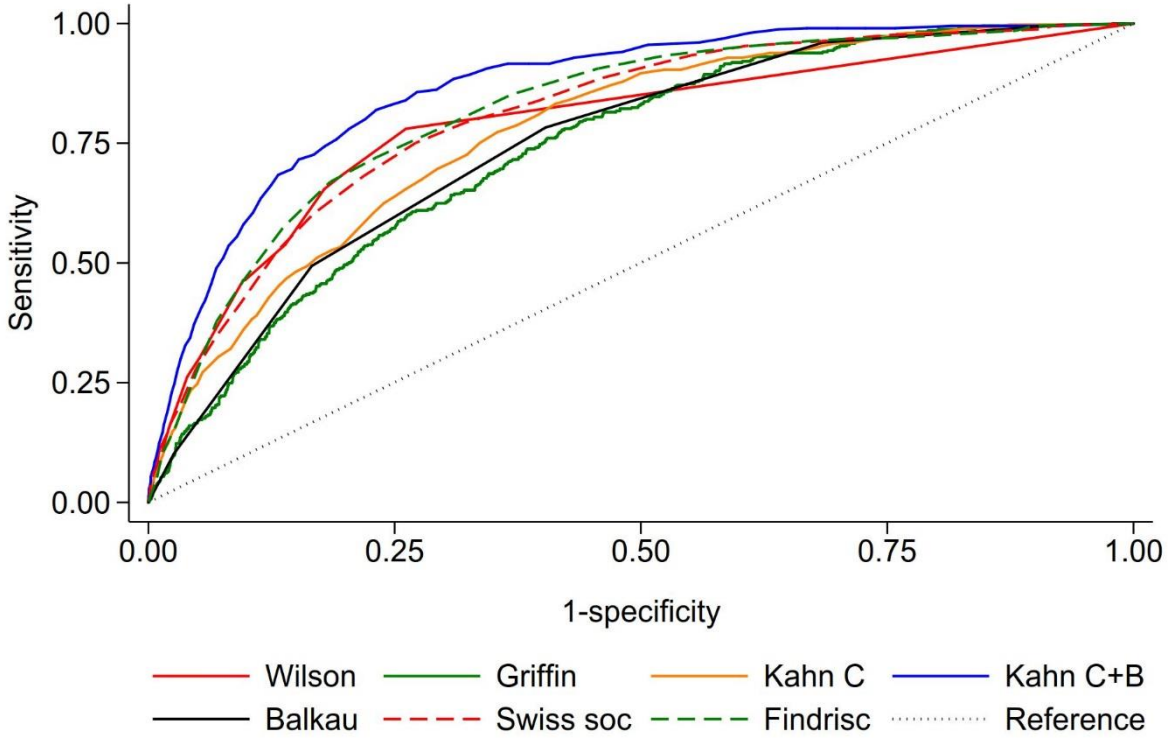


Figure 2: ROC curves of the seven diabetes risk scores.



Tables

Table 1: Factors associated with incident diabetes, 10.9-year follow-up, CoLaus study, Lausanne, Switzerland

	No diabetes	Incident diabetes	P-value
N	4726	405	
Gender (women)	2669 (56.5)	149 (36.8)	<0.001
Age (years)	51.3 ± 10.5	55.9 ± 9.8	<0.001
Clinical data			
Weight (kg)	71.3 ± 13.9	82.5 ± 14.2	<0.001
Body mass index (kg/m^2)	25.1 ± 4.0	28.7 ± 4.3	<0.001
Waist (cm)	86.7 ± 12.1	98.7 ± 11.5	<0.001
Hypertension (%)	2073 (43.9)	294 (72.6)	<0.001
Resting heart rate (bpm)	67 ± 9	69 ± 10	0.008
Family history of diabetes (%)	980 (20.7)	137 (33.8)	<0.001
High glucose (≥ 6.1 mmol/L)	1339 (28.4)	318 (78.7)	<0.001
Prescribed steroids (%)	20 (0.4)	3 (0.7)	
Lifestyle data			
Alcohol consumption (%)			<0.001
None	1254 (26.5)	107 (26.4)	
1-13 UA/week	2733 (57.8)	212 (52.4)	
14-27 UA/week	601 (12.7)	58 (14.3)	
≥28 UA/week	138 (2.9)	28 (6.9)	
Smoking categories (%)			0.001
Never	1987 (42.0)	132 (32.6)	
Former	1519 (32.1)	151 (37.3)	
Current	1220 (25.8)	122 (30.1)	
Caffeinated drinks consumption (%)			0.135
None	289 (6.1)	25 (6.2)	
1-3 u/day	3075 (65.1)	264 (65.2)	
4-6 u/day	1158 (24.5)	89 (22.0)	
>6 u/day	204 (4.3)	27 (6.7)	
Physical activity (%)	2687 (56.9)	181 (44.7)	<0.001
Blood markers			
Fasting plasma glucose (mmol/l)	5.3 ± 0.5	6.0 ± 0.6	<0.001
Triglycerides (mmol/l)	1.27 ± 0.96	1.99 ± 1.99	<0.001
HDL (mmol/l)	1.68 ± 0.44	1.46 ± 0.37	<0.001
Uric acid (µmol/l)	303 ± 81	353 ± 87	<0.001

UA, units of alcohol. Results expressed as average ± standard deviation or as number of participants and (percentage). Between-group comparisons performed using student's t-test or Kruskal-Wallis test (§) for continuous variables and chi-square or Fisher's exact test (†) for categorical variables.

Table 2: Bivariate analysis of diabetic risk scores, 10 year follow-up (2003-2006 to 2014-2017) CoLaus study, Lausanne, Switzerland

	All	**No diabetes**	**Incident diabetes**
N	5131	4726	405
Griffin et al.			
Score	11 [3 - 35]	10 [3 - 32]	38 [17 - 66]
High risk (%)	702 (13.7)	562 (11.9)	140 (34.6)
Balkau et al.			
Score	2 [1 - 3]	2 [1 - 3]	3 [3 - 4]
High risk (%)	2222 (43.3)	1905 (40.3)	317 (78.3)
Kahn et al (C)			
Median scorve	25 [12 - 40]	23 [12 - 38]	44 [32 - 57]
High risk (%)	1443 (28.1)	1184 (25.1)	259 (64.0)
Wilson et al			
Probability	3 [3 - 4]	3 [3 - 4]	7 [4 - 18]
High risk (%)	1552 (30.3)	1236 (26.2)	316 (78.0)
Swiss Diabetes association			
Score	7 [4 - 12]	7 [3 - 11]	14 [11 - 17]
High risk (%)	1586 (30.9)	1282 (27.1)	304 (75.1)
Findrisc			
Score	6 [3 - 10]	6 [3 - 9]	12 [9 - 14]
High risk (%)	1388 (27.1)	1096 (23.2)	292 (72.1)
Kahn et al (CB)			
Score	19 [9 - 33]	18 [9 - 30]	47 [35 - 56]
High risk (%)	1426 (27.8)	1094 (23.2)	332 (82.0)

Results expressed as median [interquartile range] or as number of participants and (percentage). Between-group (diabetes and non-diabetes) comparisons using Kruskal-Wallis test or chi-square test. All differences are significant at $p<0.001$

Table 3: Diagnostic performance of the diabetic risk scores, 10 year follow-up (2003-2006 to 2014-2017) CoLaus study, Lausanne, Switzerland

	AUC	Sensitivity §	Specificity §	Positive predictive value §	Negative predictive value §	Number needed to screen §§
Griffin et al.	0.740 (0.718 - 0.762)	34.6 (29.9 - 39.4)	88.1 (87.2 - 89.0)	19.9 (17.0 - 23.1)	94.0 (93.3 - 94.7)	36.7
Balkau et al.	0.750 (0.728 - 0.771)	78.3 (73.9 - 82.2)	59.7 (58.3 - 61.1)	14.3 (12.8 - 15.8)	97.0 (96.3 - 97.6)	16.2
Kahn et al (C)	0.777 (0.755 - 0.798)	64.0 (59.1 - 68.6)	74.9 (73.7 - 76.2)	17.9 (16.0 - 20.0)	96.0 (95.4 - 96.6)	19.8
Wilson et al.	0.788 (0.765 - 0.811)	78.0 (73.7 - 82.0)	73.8 (72.6 - 75.1)	20.4 (18.4 - 22.5)	97.5 (96.9 - 98.0)	16.2
Swiss Diabetes association	0.807 (0.787 - 0.828)	75.1 (70.6 - 79.2)	72.9 (71.6 - 74.1)	19.2 (17.3 - 21.2)	97.2 (96.5 - 97.7)	16.9
Findrisc	0.818 (0.798 - 0.838)	72.1 (67.5 - 76.4)	76.8 (75.6 - 78.0)	21.0 (18.9 - 23.3)	97.0 (96.4 - 97.5)	17.6
Kahn et al (CB)	0.866 (0.849 - 0.883)	82.0 (77.9 - 85.6)	76.9 (75.6 - 78.0)	23.3 (21.1 - 25.6)	98.0 (97.5 - 98.5)	15.5

Results expressed as value (95% confidence interval). § Of high vs. low risk; §§ to detect one diabetic case.

Table 4: Results of the bivariate comparison of the AUCs between diabetes risk scores.

		Model 2					
		Griffin	Kahn C	Kahn CB	Balkau	SDAS	Findrisc
Model 1	Wilson	<0.001	0.358	<0.001	0.004	0.047	0.002
	Griffin		<0.001	<0.001	0.319	<0.001	<0.001
	Kahn C			<0.001	<0.001	0.001	<0.001
	Kahn CB				<0.001	<0.001	<0.001
	Balkau					<0.001	<0.001
	SDAS						0.029

Model 1 better Model 2 better

Comparisons were performed using the **roccomp** command of Stata. SDAS, Swiss diabetes association score

Supplementary tables

Supplementary table 1: characteristics of the diabetes risk scores

	FINDRISC	Swiss Diabetes association	Wilson et al.	Griffin et al.	Balkau et al.	Kahn et al (C)	Kahn et al. (CB)
Sample size	4'435		3'140	1'077	3'817	12'729	12'279
Follow-up time	5-10 years		7 years	cross-section.	9 years	9 years	9 years
Incidence of DM	4.1%		5.1%	4.46%	5.61%	19%	19%
Sex				X	X		
Age	X	X		X		X	X
Clinical data							
BMI	X	X	X	X			
Weight						X	X
Waist	X	X			X	X	X
Height						X	X
Hypertension*	M	M	A/M	M	A/M	X	X
Resting heart rate						X	X
Family history of diabetes		X	X	X	X	X	X
Personal history of hyperglycemia	X	X					
Corticosteroids				X			
Lifestyle data							
Physical activity	X	X					
Smoking				X	X	X	
Alcohol							X
Fruit & vegetable consumption	X	X					
Blood markers							
Glucose			X				X
Triglycerides			X				X
High density lipoprotein			X				X
Uric acid							X
Score threshold	≥ 9 pts	≥ 9 pts	24 pts	37%	≥5 pts	≥38 pts	≥38 pts
Risk of developing T2DM	13%	13%	33%	37%	30%	17.7%	17.7%

BMI, body mass index ; T2DM, type 2 diabetes mellitus. *A: anamnestic, M: antihypertension medication

Supplementary table 2: Characteristics of included and excluded participants. 10-year follow-up (2003-2006 to 2009-2012) CoLaus study, Lausanne, Switzerland

	Included	Excluded	P-value
N	5131	1602	
Gender (Woman %)	2818 (54.9)	726 (45.3)	<0.001
Age (years)	51.7 ± 10.5	55.4 ± 11.1	<0.001
Clinical data			
Weight (kg)	72.2 ± 14.2	77.0 ± 17.0	<0.001
Body mass index (kg/m^2)	25.4 ± 4.2	27.2 ± 5.3	<0.001
Waist (cm)	87.6 ± 12.5	93.6 ± 14.7	<0.001
Hypertension (%)	2367 (46.1)	1011 (63.4)	<0.001
Resting heart rate (bpm)	67 ± 9	70 ± 11	<0.001
Family history of diabetes (%)	1117 (21.8)	455 (28.4)	<0.001
Prescribed steroids (%)	23 (0.5)	2 (0.1)	0.095†
Lifestyle data			
Physical activity (%)	2868 (55.9)	727 (45.6)	<0.001
Alcohol consumption (%)			<0.001
None	1361 (26.5)	554 (34.6)	
1-13 UA/week	2945 (57.4)	708 (44.2)	
14-27 UA/week	659 (12.8)	254 (15.9)	
≥28 UA/week	166 (3.2)	86 (5.4)	
Smoking categories (%)			0.024
Never	2119 (41.3)	613 (38.4)	
Former	1670 (32.6)	513 (32.1)	
Current	1342 (26.2)	470 (29.5)	
Blood markers			
Fasting plasma glucose (mmol/l)	5.3 ± 0.6	6.2 ± 2	<0.001
Triglycerides (mmol/l)	1.33 ± 1.09	1.60 ± 1.39	<0.001 §
HDL (mmol/l)	1.66 ± 0.44	1.54 ± 0.43	<0.001
Uric acid (µmol/l)	307 ± 83	328 ± 89	<0.001

UA, units of alcohol. Results expressed as average ± standard deviation or as number of participants and (percentage). Between-group comparisons performed using student's t-test or Kruskal-Wallis test (§) for continuous variables and chi-square or Fisher's exact test (†) for categorical variables.